UNIVERSITY OF GONDAR
COLLEGE OF MEDICINE AND HEALTH SCIENCE
DEPARTMENT OF INTERNAL MEDICINE

INCIDENCE AND PREDICTORS OF TUBERCULOSIS AMONG ADULT PEOPLE LIVING WITH HIV IN AFAR HEALTH FACILITIES, NORTHEAST ETHIOPIA

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Examiner

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ACRONYMS

AHR	Adjusted hazard ratio
AIDS	Acquired immune deficiency syndrome
ART	Anti Retroviral Therapy
ARHO	Afar regional health office
ATT	Anti tuberculosis therapy
BMI	Body mass index
CI	Confidence interval
CPT	Co trimaxazole prophylaxis therapy
ECSA	Ethiopian central statistical agency
FMOH	Federal ministry of health
HIV	Human immune deficiency virus
HAART	Highly active anti retro viral therapy
Hgb	Hemoglobin
INH	Isoniazid
IQR	Inter quartile range
IPT	Isoniazid prophylaxis therapy
IRIS	Immune reconstitution inflammatory syndrome
MTB	Mycobacterium tuberculosis
OR	Odds ratio
RR	Relative risk
PLHIV	People living with HIV/AIDS
SPSS	statistical package for social science
UNAIDS	United nation joint program on HIV/AIDS
WHO	world health organization

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ABSTRACT

Background: Tuberculosis (TB) and human immune deficiency virus (HIV) infections are two major public health problems in many parts of the world .TB is the leading cause of morbidity and mortality among HIV-infected individuals.

Objective: To assess incidence and predictors of tuberculosis among PLHIV in afar heath facilities, northeast Ethiopia 2015.

Methods: A retrospective follow up study was conducted among 503 adult (age>15 years) PLHIV who enrolled in HIV care clinic from July 1, 2010 to June 30, 2011. Ethical clearance was obtained from school of medicine. Data collected from patient records. Data checked for completeness and entered to EPI-INFO version 7 then exported to SPSS version 20 for further analysis. Bi-variate and multivariate Cox proportional model were fitted to investigate predictors. p value <0.05 in the multivariate Cox proportional hazards model independently associated with the outcome variable.

Result: of all the 503 charts reviewed, 451 charts were included in the analysis. For a total of 1377.30 Person Years (PY) of observation, 119(26.38%) developed TB. The overall incidence density of TB was 8.6 cases per 100PY. Sixty-eight (57.14%) of TB developed at the first year of follow up. Past TB history (AHR=2.32, 95%CI=1.511-3.573). Ambulatory and bedridden functional status at baseline (AHR=2.42, 95%CI(1.05-5.59) ,(AHR=2.42 ,95%CI=(1.56-3.75). Baseline BMI<18.5kg/m^2 (AHR=1.621, 95 %CI =1.09-2.40).Not take IP (Isoniazid prophylaxis therapy) (AHR= 6.96,95%CI=2.53-19.08). Baseline Hgb <12.5g/dl and Hgb <10 g/dl (AHR=2.00, 95% CI=1.08-3.71), (AHR= 2.54, 95%CI=1.57-4.11) respectively were predictors that associated for TB occurrence.

Conclusion and recommendations: TB incidence in adult PLHIV remains high. Past TB history, Not receiving IPT, low BMI, low Hgb and unable to work was the most significant predictors for occurrence of TB. The high incidence of TB finding in this study call for an improved TB/HIV activity and scale up of IPT to reduce risk of TB is advisable.

Key words: Afar, HIV, Incidence, tuberculosis, northeast

1. INTRODUCTION

1.1 Statement of the problem

Tuberculosis (TB) is a chronic infectious disease caused by mycobacterium tuberculosis (MTB).It typically affects the lung but also can affect other parts of the body as well(1). TB and human immune deficiency virus (HIV) infections are the two leading public health problems in many parts of the world(2, 3). Since the beginning of the later pandemic, nearly 78 million people have contracted HIV and close to 39 million have died of AIDS causes. In 2013, an estimated 2.1 million people were newly infected with HIV. More- than two-thirds (70%) of all people with HIV, 24.7million, live in sub-Saharan Africa and 1.5 million people in the region become newly infected in 2013(3, 4).

Globally about a third of world's population was estimated to be infected with tubercle bacilli and hence at risk of developing active TB disease(1). It ranks as the second leading cause of death from a single infectious agent, after HIV(2, 4). In 2013 globally 9 million people develop incident cases of TB and 12 million prevalent TB cases and 1.5 million people died from TB. The 22 high burden countries accounted for 82% of all estimated cases worldwide(4).

Worldwide, TB was a leading cause of death among people living with HIV and HIV was the most potent risk factor for the development of tuberculosis. According to WHO report 2014, 1.1 million incident TB cases are among people living with HIV. In 2013, 1.5 million people died from TB, including 360,000 among people who were HIV-Positive. The prevalence of TB-HIV Co-infection is higher worldwide and 90% of these co-infected cases live in developing nations(4). Developing nations are the home of this deadly tied disease. Sub-Saharan Africa accounted for 79% of the burden of TB-HIV co infections, followed by South-East Asia (11%). In the African region that has the highest TB/HIV burden, three out of four TB patients knew their HIV status Globally,70%of the TB patients known to be living with HIV in 2013 were started on antiretroviral therapy (ART).In 2013, 5.5 million people enrolled in HIV care were screened for TB, up from 4.1million in 2012. Of the people newly enrolled in HIV care in 2013, 0.6 million were provided with ionized preventive therapy(4-6).

Even though tuberculosis is the most commonly diagnosed opportunistic infection and disease in HIV infected individuals which can be curable and reduced with appropriate measure of therapy but hidden TB can hasten the progression of HIV(6). The presence of TB may affect individuals with HIV infection in numerous ways .TB increase T-cell replication and it increases HIV replication and it leads to increased viral load. TB facilitate occurrence of other opportunistic infections(7) .It also challenging to diagnose TB with HIV because the clinical manifestations of TB in HIV infected individuals are somewhat different. The life time risk of HIV infected individuals to develop TB is 20-37 times greater than HIV negative individuals to develop active TB from the latent infection of mycobacterium tuberculosis(4, 8).

The dangerous synergy affects all aspects of both diseases, from pathogenesis and the epidemiologic profile, to clinical presentation, treatment, and prevention(6). This synergy also impacts largely the management of individuals co-infected with this deadly disease related to pill burden ,drug to drug interaction ,increased adverse effect and immune reconstitution inflammatory syndrome(IRIS.As a result, TB become the leading opportunistic infection that cause of death among HIV infected people. This factors and late diagnosis of TB highly contribute to keep the mortality rate of TB very high among the co-infected people (6, 7).

The WHO has classified Ethiopia 7th among the 22 high burden countries with TB .According the WHO Global report 2013, Ethiopia had an estimated 200,000 TB cases in 2011 with an estimated incidence TB cases of 258/100,000 population. TB mortality rate is 18/100,000 and the prevalence of all forms TB is estimated to be 237/100,000. According to WHO Global report 2014, Ethiopia remains in the list of the country's most heavily affected TB with prevalent cases of around 200,000 ,224/100,000 and incidence cases of 211per 100,000. Also Ethiopia is among countries having high TB and HIV co infection rate(5). There are more than1 million people living with HIV virus in the country and roughly about 40-70% of HIV patients in Ethiopia are co-infected with TB. This Synergy also impacts largely the co infected individual's social, economical and healthy aspects than those patients with only HIV infection(4, 8). Moreover, TB and HIV co-infection are associated with special diagnostic and therapeutic challenges and

constitute an immense burden on healthcare systems of heavily infected countries like Ethiopia.

Great efforts have been made in line with millennium development goals (MDG) and post 2015 TB related programs to combat TB/HIV in the last two decades. However, this collaborative activity is not uniformly effective on all the different socio demographic variations and limited resources areas in nearly isolated setting .Also the burden is not equally distributed in various socio demographic setting and this unequivocal distribution demands a research to determine the incidence and to pick the potential predictors associated with TB in order to identify potential risks and to improve prevention service in the venerable groups.

Therefore, studying the incidence and predictors of TB among HIV infected people on the nearly isolated setting will have a great value to continue the collaborative activity to hit the deadly epidemic and to improve the health care system in taking appropriate action in identifying the predictors and alarming the partners and responsible body to give attention to the nearly isolated setting.

1.2. Literature review

1.2.1. Incidence of TB among PLHIV

Several studies conducted in different places of the world showed the synergic effect of TB and HIV among HIV infected patients. A large study conducted on synergic(7) interaction between HIV and TB epidemics showed that HIV-associated TB contributes substantially to the burden of TB-associated morbidity and mortality(9). HIV infection is the strongest known risk factor for TB. High HIV prevalence rates are significantly correlated with high TB incidence rate. Urban population growth escalates the HIV and TB Syndemic in developing countries. The association between poverty, urbanization, housing density, and TB incidence is highly related (7, 10). Globalization and increased population mobility have shaped the HIV-TB syndemic. Individuals with a new diagnosis of TB are nearly 19 times more likely to be co infected with HIV than those without TB (0.8% HIV and 15% HIV prevalence in incident TB cases *(11)*. Conversely, people living with HIV are 20 to 30 times more likely to develop TB than those without HIV.In developed nations the incident cases of TB was increased with the HIV epidemic on HIV infected patients. In developing country the synergic effect is worse than the developed nations (12). HIV affects and alters TB transmission, duration of infectiousness and progression of disease. Similarly, HIV increases the risk of progression to active TB in both primary and latent TB. For HIV-uninfected individuals with latent TB infection (LTBI), the life-time risk of developing active TB due to reactivation is 8 to10%. In contrast, this risk is approximately 10% per year for HIV-infected persons(13). Other studies showed that, ART reduces the incidence of TB among HIV infected patients but it associated with risk of TB-IRIS, adverse effects, pill burden and disease progression (6, 14, 15).

According to a retrospective cohort study in Israel, conducted among 6579 PLHIV reported between 1983 and 2010, corresponding to 55737 person-years, 384 (5.8%) developed tuberculosis. The overall tuberculosis incidence-density was 6.9 cases/1000 person-years (95% CI 1.8–12.0). The cumulative tuberculosis-incidence among PLHIV in 2010 was 586 times higher than in HIV-negative individuals (3400 and 5.8 cases per

100000 populations, respectively). .Majority of cases were immigrants came from endemic countries(16).

From studies done in Malaysia, related to TB/HIV revealed that there is a rise in the incidence of tuberculosis cases among HIV infected patients since 2011. Similarly, a two-year multi-centered study found that, the co-infection rate among patients was estimated about 7.7%and TB incidence rate was 1.8 cases per1000 PY. HIV patients had greater rates of pulmonary tuberculosis (68-79%) and lesser rates of extra pulmonary tuberculosis(17).

A cohort study conducted among 908 Mexican participants PLHIV followed for a total of 3032.7 person-years showed that, there were 59 (6.5%) cases of incident tuberculosis during follow up (1.95 cases per 100 person-years (95% CI= 1.51-2.50) (18) .similarly in a retrospective medical record based study conducted in Korea among total of 1,301 HIV-infected patients observed between January 1998 and December 2010 revealed that, Eighty-four patients were diagnosed as having TB during the study period, seventy (5.4%) of patients were newly diagnosed during the study period with incidence rate of 1.23 cases per 100 PY. Initial CD4+ cell count <200 cells/μl at the time of enrollment was independently associated with an increased incidence of TB(19).

A study conducted among household contacts in south Africa showed that, the overall TB incidence rate was 1.3 per 100 person years (95% CI= 0.9-1.9/100py) and TB incidence for individuals who were HIV-infected and HIV sero-negative at baseline was 5.4/100py (95%= CI 2.9-9.0/100py) and 0.7/100py (95% CI= 0.3-1.4/100py), respectively.(20).

A 2 year prospective study done in Tanzania among both ART and Pre-ART groups of 67, 686 patients 7602 patients were diagnosed with active TB. The TB incidence rate was 7.9 [95% confidence interval (95% CI= 7.6-8.2] per 100 person-years prior to ART initiation, and 4.4 (95% CI= 4.2-4.4) per 100 person-years for patients receiving ART. Risk factors for incident TB included being male, having low BMI or middle upper arm circumference, lower CD4 cell count and advanced WHO disease stage(21). Similarly an eight year follow up study done in sub- Saharan Africa among 7114 HIV positive

patients enrolled, During follow-up, 421 incident tuberculosis cases were notified with an estimated incidence of 3.6 per 100 P-Y [95% (CI= 3.26-3.97]. The incidence rate varied over time and increased significantly from 2.96 to 43.98 cases per 100 p-y. Poor clinical condition at baseline (Hazard Ratio (HR) 3.89, 95% CI =2.87-5.28), WHO clinical stage 3 or 4 (HR 2.48, 95% CI= 1.88-3.26), being anti-retroviral naive (HR 2.97, 95% CI= 2.25-3.94 (22).

Like other studies in Africa studies conducted in Ethiopia among PLHIV revealed that incidence of TB was high. According to retrospective cohort study done in northwest Ethiopia, showed that incidence of TB were 7.9 cases per 100 PY. The median time for development of incident TB during the follow-up was 9.5 months (IQR, 5.5-16.5 months. Majority of the incident TB occurred within the first year of follow up(23). Similarly, studies done in west part of Ethiopia found that incidence rate of TB during follow up among 588 patients on pre-ART care was an overall incidence of 3.78 cases per 100 PY. The incidence rate was higher among non-IPT users(5.06 per 100 PY but it was 2.22 per 100 PY in IPT user group (24) .Likewise , studies from Assella hospital revealed that, incidence of TB among HIV positive individuals on HAART was 3.73 cases of TB per 100 person year while it was 7.02/100 PY among individuals on pre HAART follow up(25).

1.2.2 Predictors of tuberculosis among adult PLHIV

There are various reported risk factors for the development of TB among adult PLHIV. These factors can be classified and described as socio demographic, clinical, treatment related and nutrition related factors and like. Similar to HIV negative people with TB cases adult males predominate in having TB with HIV in studies done in previous studies (16, 19, 26). Still there are multiple studies which showed to the contrary(18, 27). Younger age was also found to be a common determinant factor as compared to those above 40 years of age(16, 18). But few studies found that advanced age was risk factor for developing it (19, 27). Considering residence, urban residents were found to be more risk factor for TB among HIV infected patients(28). Some behavioral factors (substance use) like alcoholism, cigarette smoking was associated with treatment failure among HIV infected patients indirectly increased the risk of TB among the HIV infected

patients (16, 17). Also, previous history of TB found to be a determinant factor for TB development among HIV infected patients((16). As TB is an opportunistic disease, low CD4 count and advanced WHO clinical stage at base line were highly associated with development of TB .Low CD4 count was one of the strongest determinant factor among this group(17, 23, 26).

In addition, other risk factors like diabetes mellitus, chronic kidney disease, functional status and presence of other opportunistic were significantly associated with reactivation and development of active TB among HIV infected people(16, 28, 29).

Another study revealed that having a low BMI is a risk for development of TB among HIV patients(21). In a seven year study conducted among adult PLHIV in Dares Salaam, Tanzania, showed that 976 HIV patients enrolled to the follow up 9.4% were develop active TB throughout the prospective follow up. The study revealed that baseline BMI, Year 1 BMI and change in BMI from baseline to Year 1 were all significantly and independently associated with the risk of developing TB during prospective follow-up. Patients with a baseline BMI < 17 kg/m^2 had a greater risk of developing TB during prospective follow-up (HR 3.72, 95%CI =1.16–12.0, P= 0.028. Also, patients whose BMI fell by >0.5 kg/m^2 from baseline to Year 1 had a greater risk of developing TB (HR 2.03, 95%CI 1.29–3.20, P= 0.002. likewise, a cohort study in Uganda revealed that hemoglobin of ≤10 mg/dl, BMI ≤15.5 kg/m^2, and opportunistic infections other than TB were significant risk factors for the development of TB among this group(20, 21, 30-33).

Different studies also, showed that use of IPT, ART and CPT reduces the risk of active TB in HIV-infected individuals., treatment of latent TB infection (LTBI) in HIV-infected individuals helps to reduced the risk of active TB by 32% (risk ratio (RR) 0.68; 95% confidence interval (CI= 0.54 - 0.85)(24, 34, 35).The use of ART in HIV-infected adults also magnificently reduces the incidence of TB. Also, patients starting ART earlier, at higher CD4 cell counts, have a 2-fold lower risk of TB compared with those initiating ART at lower CD4 cell counts(29, 36). Similar result was revealed from a in south Africa with, a 37% reduction in the risk of TB was evident in individuals receiving IPT and ART

compared with patients receiving ART only (RR 0.63)(22). As part of a comprehensive HIV Care package, all HIV and TB clinics should benefited from co-trimoxazole prophylaxis concurrent use with other medications like HAART, anti-tuberculosis drugs and drugs that treat other opportunistic infections by giving especial attention to signs of side effects and adherence(37, 38).

Studies conducted in Ethiopia revealed that, several determinant factors associated for incidence of TB among HIV infected people. In almost all studies young age groups were the predominant risk group to develop incident tuberculosis (39). Inline to studies in Africa females and urban residents were more risk to develop TB than males and rural residents (24, 25). HIV infected individuals who had not attended formal education were found to be 4.5 times more likely to develop TB than those who attended formal education, OR = 4.55, 95% CI(2.09- 9.90)(39).Low CD4 cell count (<200cell/mm3) and advanced WHO clinical stages and unable to work in functional status were independently associated to develop active TB than those HIV infected individuals with CD4 count of >500cells/ mm3, early WHO clinical stages and able to work(23, 40). Having low hemoglobin level < 10mg/d , OR = 2.96, 95% CI= (1.28, 6.80),and Having BMI <18.5 kg/ m^2 were found to be significantly associated with TB infection, OR = 3.80, 95% CI =2.39,6.08)(40).Patients with diabetic mellitus and being pre-ART were more likely infected with TB, OR = 3.53, 95% CI =1.55, 8.07) but being on INH preventive therapy (IPT) treatment was marginally associated with tuberculosis co-infection(39, 40) . in the contrary IPT was independently associated with incidence of TB(24).

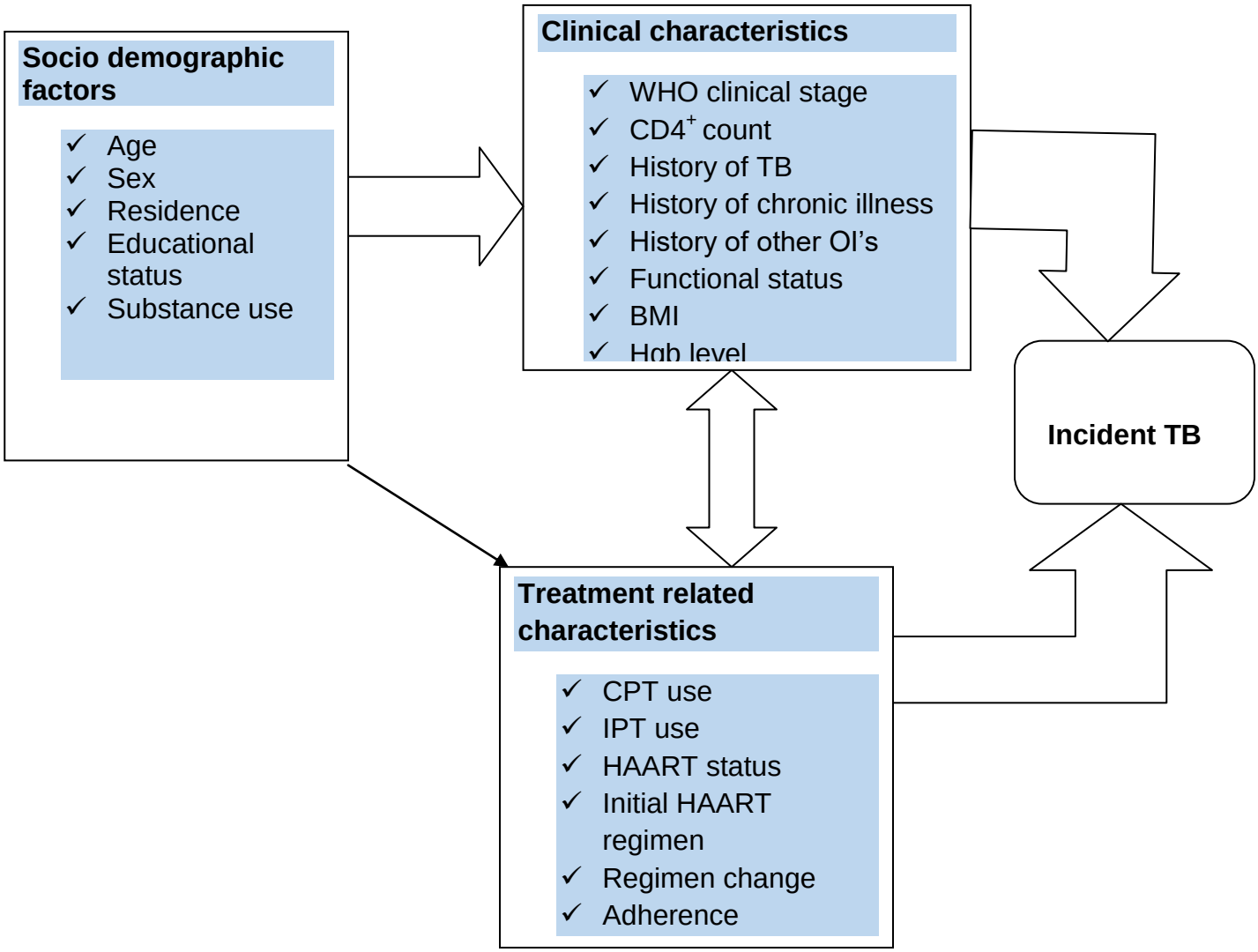

Figure1. Conceptual frame work of incidence of TB among Adult PLHIV (this developed from variable in the Literature review)

1.3. Justification of the study

Tuberculosis is the main cause of morbidity and mortality among HIV infected people. It also enhances the burden of other opportunistic infections. TB co- infection in HIV infected individuals causes several problems on the patient like adverse effect of medication, pill burden and drug to drug interaction with the pre existing HAART and other OI's medications.

In the study setting no study has been conducted. Therefore it will enrich the existing level of evidence by closing the place gap in information and it will help policy makers and stake holders to strengthen the TB/HIV prevention and control programs in the set up. Moreover, it helps to show the gab to the partners and responsible body working on the TB/HIV collaborative activity.

2. OBJECTIVE

2.1 General Objective

The aim of this study is to assess the incidence and predictors of tuberculosis among adult people living with HIV in Afar public health facilities, northeast Ethiopia 2015.

2.2 Specific Objectives

- To determine incidence rate of tuberculosis among adult people living with HIV in afar public health facilities, northeast Ethiopia 2015.
- To identify predictors of tuberculosis occurrence among adult people living with HIV in afar public health facilities, northeast Ethiopia 2015.

3. METHODS

3.1 Study design

Institution based retrospective cohort follow-up study design was employed to assess the incidence and predictors of tuberculosis among adult people living with HIV.

3.2 Study area and period

Data was collected from May to Jun, 2015 in Afar national regional state selected health facilities. Afar is located in the North-eastern part of Ethiopia. The region has a population of 1,678,000 only 289,000 population live in urban and semi urban area(41). Administratively the region consists of five administrative zones with 32 districts with 28 urban and 401 rural counties (Kebeles). The capital city of the region (Samara) is located 536 km away from Addis Ababa. In Afar there are four hospitals, 40 health centers, 270 health posts and 15 private clinics delivering health services for the people living in the region. HIV care service introduced in the region in 2006/7. According recent report 15 health institutions provide HIV chronic care and support service for around 4,000 PLHIV. The study sites selected based on their number of client follow and presence of TB and HIV follow up clinic. Based on this, the study was focused on two health centers (Awash, and Samara), Asayta hospital, Abala hospital and the only general hospital (Dubti) in the region. These health institutions provide chronic HIV care and follow up for about 70% of patients living with HIV in the region.

3.3 Source population

The source population of the study was all adults PLHIV who had enrolled to chronic HIV care and support program in Afar health facilities.

3.4 study population

The study population was those adults PLHIV who are enrolled to chronic HIV care from July1, 2010 to June 30, 2011 in afar public health facilities (Dubti hospital, Asayta hospital, Abala hospital, and Awash and Samara health center.

3.5 Inclusion and exclusion criteria

Inclusion criteria:

- ✓ All adult PLHIV who enrolled newly in to chronic adult HIV care clinic from July 1, 2010 to June 30, 2011.

Exclusion criteria:

- ✓ PLHIV on HIV care clinic with incomplete information (date of enrollment, baseline CD4 count and transfer in patients and patients with TB in the last 3 month was excluded.

3.6 sample size

To determine the sample size for incidence of TB among HIV infected people single population proportion formula assuming 95% confidence interval (CI) and 5% margin of error (d) will be used. Considering prevalence of TB among HIV infected patients to be 13% from the national figure but according to studies done in Jimma the prevalence is 17%, then(42).

n=initial sample size =

$$\mathrm{n} = (Z\alpha/2)^2 \frac{p(1-pP)}{d^2}$$

$$= (1.96)^2(0.17)\ (0.83)/(0.05)^2$$

$$=217$$

To determine the sample size for the second objective, two proportion population formula will be employed .Several studies indicated that base line CD4 ,WHO clinical stage and BMI are the best predictors of incident TB among HIV infected patients. Based on this assumption using EPI Info stata calcu sample size will be determined at 95% CI ,80% power of test will be calculated for the key predictors from the previous studies(CD4 count <100,WHO clinical stage III or IV and BMI <18.5)(21, 40).

Table 1: sample size calculation

No	Key predictors	Assumption	Odds ratio/hazard ratio	Sample size
1	Advanced WHO stage	At 95% CI and power 80%	2.0 9 (1.33, 3.28)	291
2	Baseline CD4>200cell/ml	At 95% CI and power 80%	2.35(1.23, 4.48)	290
3	Baseline BMI <18.5	At 95% CI and power 80%	3.85(2.39, 6.08)	98

As shown on the table sample size for similar calculations was employed for other exposure variables (educational status, age, sex, past TB) and the sample size calculated for predictors is greater than the sample size estimated on proportion .so, the two population proportion sample size was maximum number 291 and it will be taken as the final sample size for this the study; by considering 3.3% (40) of expected incomplete records the final sample size 301.

But for this study for sake of better statistical power, all the records **503** were reviewed.

3.7 sampling procedure

All adult people living with HIV who was enrolled from July 1, 2010 to June 30, 2011 to adult chronic care clinics of the selected health facilities was included in the study and looking their five year follow up till May15, 2015.

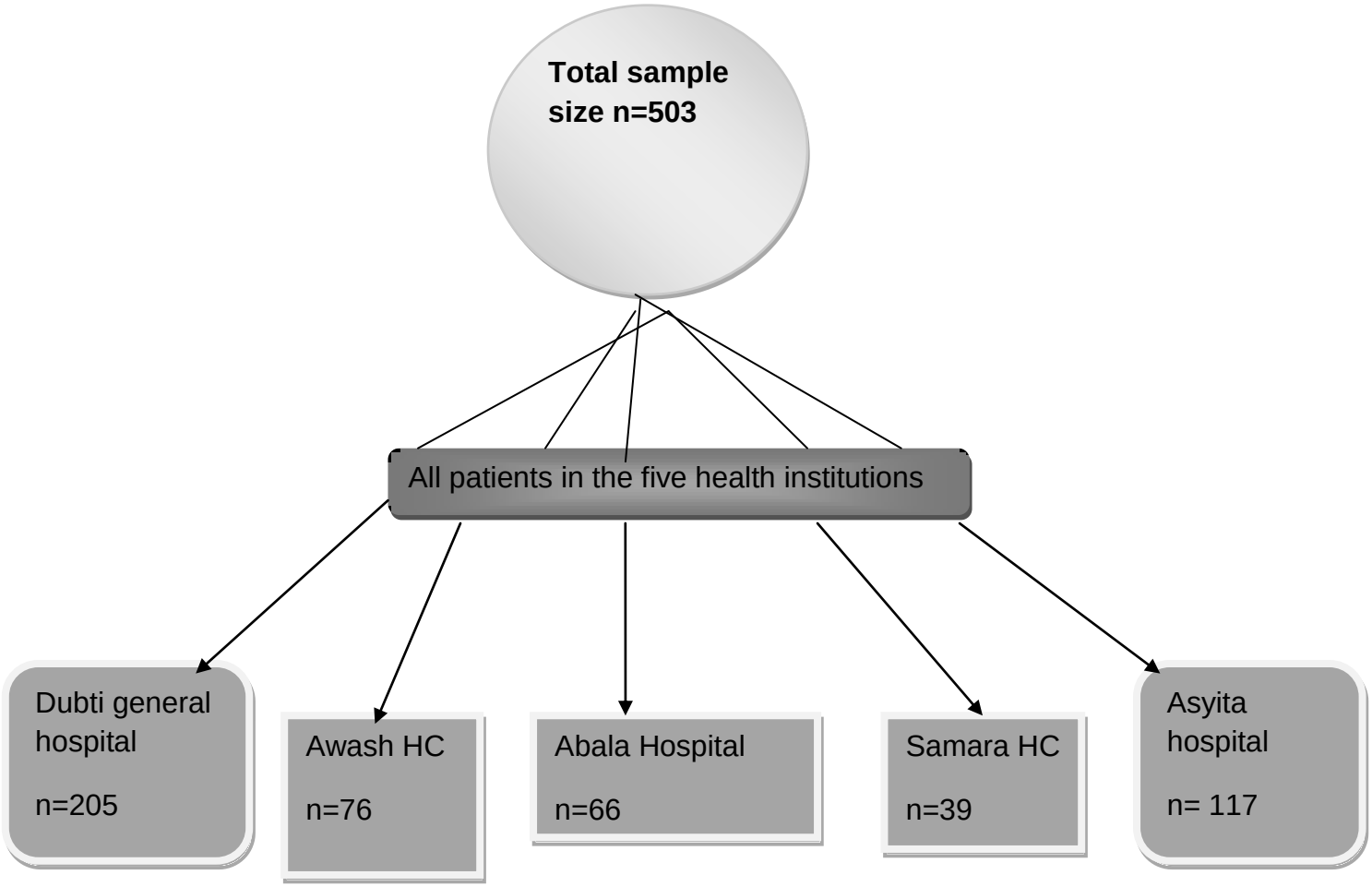

Figure 2. Schematic presentation of the selected health facilities

The total sample size was taken from the above five health facilities. All the study subjects found during data collection included in the study.

3.8 Data collection method

Available information on the patient chart was observed and suitable data extraction format was prepared in English. Subsequently, the data was collected by four diploma nurses and two BSc nurses who had ART training using the data collection format from the patient records. Data clerk of each health facility and case managers assisted the data collators by identifying the charts. Charts were retrieved by using the patient medical record number and ART registration number which is found on the data base of the health facilities.

3.9 Data quality assurance

Quality of data was maintained by recruiting data collectors and supervisors who had ART training. One and half day comprehensive training was given for data collectors and supervisors prior to actual data collection on the objective of the study and how to collect data from the charts using the format prepared for the study purpose. Concise information about the variables on the format and patient charts .Data collection tool was pre tested for consistency of review tools and completeness of understanding the review tools and completeness of data items on 10% charts at logia health center. The retrieval process was closely monitored by the two supervisors and by the principal investigators on daily bases throughout the data collection period .Completed forms were checked regularly for completeness of information and any slit immediately identified and correction measure was taken.

3.10 study variables

3.10.1 Dependent variable

- ✓ **incidence of TB**

3.10.2 Independent variable

Socio demographic characteristics:

- ✓ Age
- ✓ Sex
- ✓ Residence
- ✓ Educational status
- ✓ Substance use

Clinical factors

- ➢ WHO clinical stage
- ➢ CD4 count
- ➢ Chronic illness
- ➢ Previous TB history
- ➢ Functional status
- ➢ other opportunistic infection
- ➢ BMI
- ➢ Hemoglobin level

Follow up and treatment related characteristics**:**

- ART status
- Initial HAART regimen
- Initial regimen change
- Co-trimaxazole prophylaxis therapy
- INH prophylaxis
- Adherence

3.11. Operational definition

Chronic illness: - Non AIDS defining chronic illness like DM, Kidney disease and malignance

CPT prophylaxis: - A patient who took co-trimaxazole for greater than 1 month for prophylaxis purpose.

Event or incident TB:-any form of TB that diagnosed clinically or radigraphicaly or laboratory confirmed or patients who start anti TB empirically after enrollment.

INH Prophylaxis:-A patient who took INH alone for a purpose of TB prevention more than 3 month

Substance use:-In this study substance use is considered as any substance use recorded in the intake form of the patient chart

Censored :-participants, who did not develop the event till the end of the study or died, transfer out or drop out from follow up without having the event.

3.12 Data processing and analysis

After the data checked and cleaned for its completeness, it was entered to EPI-INFO version 7 and exported to SPSS version 20 for further analysis. Statistical summary was applied to describe socio demographic, clinical and follow up variables. Magnitude will be calculated and described by frequency and tables. Incidence density rate was calculated for the study period. Kaplan Meier was used to compare different categories of survival probability respectively. Bi-variable and multivariate Cox regression model was used to identify the predictors. Variables with value of p <0.2 in the bi-variable

analysis was candidate for multivariate proportional hazard model.95% CI of hazard ratio was computed .variables having p value <0.05 in the multivariate Cox proportional hazards model was taken as significant and independently associated with the outcome variable. The model fitness was checked with graphical and residual tests.

3.13 Dissemination of finding

Finding of the study was submitted to department of internal medicine, college of medicine and health science, university of Gondar. It will also present to University of Gondar. The dissemination also goes to afar regional health office, Dubti hospital, Asayta hospital, Abala hospital, Awash, and Samara health center and other stakeholders.

In addition possible effort will be made to present the findings of the study in different professional meetings/conferences and the manuscript will be sent to journals for publication.

3.14 Ethical consideration

Ethical Clarence was obtained from the IRB of the institute of school of medicine, university of Gondar. Permission was obtained from the ARHO and written permission letter was sent to each health facilities to conduct this research. Unique identification information was not collected on the extraction format and for all information taken from the chart confidentiality and security issue was maintained. The collected information was only used for the study purpose.

4. RESULTS

4.1 Baseline socio-demographic characteristics of PLHIV

A total of 503 records of PLHIV who were enrolled from July 1, 2010 to June 30, 2011 were reviewed. Fifty two (10.44%) of them were not included in the analysis due to incomplete information. Among the 451 patients remaining in the analysis the mean age (SD) was 32.55±7.48) and almost two third 297(65.9%) of them were below the age of 35 years. The data were collected from five health institutions urban residents were 410 (90.9%).More than half 267(59.2%) of PLHIV were females and 275 (61%) were also Muslim in religion.

At most half 234(51.9%) of patients were self employed. One hundred thirty (28.8%) patients recorded as substance users either of drugs 20% or tobacco 3.1% or alcohol 5.7% .Majority, 374(93.1%) of the patients were living in family size of 1-5.Almost half 212(47%) of the patients never went to formal education. More than two third (68.1%) of the patients were currently or formerly married.

Table 2 Socio -demographic characteristics of PLHIV enrolled to chronic HIV care at Afar health facilities, northeast Ethiopia June 30, 2015,

Characteristics		Frequency (n=451	Percent%
Age			
	15-24	55	12.2
	25-34	242	53.7
	35-44	119	26.4
	45 and above	35	7.8
Sex			
	Male	184	40.8
	Female	267	59.2
Marital status			
	never married	144	31.9
	Married	200	44.3
	divorced/separated	77	17.1
	Widowed	30	6.7
Residence			
	Urban	410	90.9
	Rural	41	9.1
Religion			
	Muslim	275	61.0
	Orthodox	165	36.6
	Others	11	2.4
Educational status			
	no formal education	212	47.0
	Primary	177	39.2
	secondary and above	62	13.7
Family size			
	1-3	216	47.9
	4-5	159	35.3
	>5	76	16.9
Occupational status			
	self employed	234	51.9
	government employed	45	10.0
	no employment	172	38.1
Substance Use			
	Users	130	28.8
	non users	321	71.2

4.2. Baseline clinical and HIV related follow up characteristics of PLHIV

From the total of 451 study participants (53.4%) had a baseline WHO clinical stage III and IV. Majority 366(81.2%) of Participants were enrolled with working functional status. Participants had baseline median CD4 cell count of 285 cell/ml(IQR178-383) at enrollment. Almost half 218(48.3%) of the participants were enrolled with BMI <18.5. 270(59.9%) study subjects had a baseline Hgb<12.5. During the follow up majority 413(91.8%) of the participants provided with CPT but only 94(20.8%) of the participants received IPT.

The eligibility criteria for the initiation of HAART was mainly WHO clinical stage 183(40.6%) and both WHO clinical stage and CD4 cell count 167(37 %.) respectively. The initial regimen frequently prescribed for the study participants were a combination of TDF,3TC and EFV 170(37.7%)followed with AZT,3TC and EFV110(24.4%) . Ninety six (21.3%) of participants changed their initial regimen.92(95.8%) of change was substitution and only 4(4.2%) patients switched to second line .majority of the drug changes was made following the development of side effect 50(52.08%) and 29(30.2%) changes was following development of TB.

Table 3. Baseline clinical and HIV related follow up characteristics of PLWHA in Afar health facilities north east Ethiopia 2015.

Characteristics	Number(n=451	Percent
Past TB		
Yes	74	16.4
No	377	83.6
OI*		
Yes	34	7.5
No	417	92.5
Chronic illness		
Yes	35	7.8
No	416	92.8
Base line functional status		
Working	366	81.2
Ambulatory and bedridden	85	18.8
BMI		
<18.5	218	48.3
≥18.5	203	45.0
WHO clinical stage		
I	62	13.7
II	138	32.8
III	172	38.1
IV	69	15.3

Table 3. Baseline clinical and HIV related follow up characteristics of PLHIV in Afar health facilities, northeast Ethiopia 2015 continued ……

Hgb level		
<10	56	12.4
10-12.49	214	47.5
≥12.5	181	40.1
CD4 count		
<100	44	9.8
100-200	124	27.5
200-349	125	27.7
≥350	158	35.0
Initial regimen		
d4t-3TC-NVP	65	14.4
AZT-3TC-EFV	89	19.7
AZT-3TC-NVP	110	24.4
TDF-3TC-EFV	170	37.7
Others♣	17	3.8
Eligibility criteria		
CD4 cell count	62	13.7
WHO clinical stage	183	40.7
CD4 count and WHO stage	167	37.0
Unrecorded	39	8.6
CPT use		
Yes	413	91.6
No	38	8.4
IPT use		
Yes	94	20.8
No	357	79.2
Did regimen changed		
Yes	96	21.3
No	355	78.7
Type of the changed regimen		
First line	92	20.4
Second line	4	0.9
Reason for change		
Tuberculosis	29	6.4
Side effect	50	11.
Failure	4	0.9
Others♣♣	13	2.9
Adherence		
Consistent	351	77.8
Inconsistent	100	22.2

OI*=other than TB, others♣, d4t-3TC-EFV, TDF-3TC-NVP&ABC-3TC-EFV

4.3 TB incidence rate

Four hundred fifty one study participants were followed for different periods in the follow up for a total of 1377.303 Person Years of observation. One hundred nineteen (26.4%) of participants develop TB while on follow up and 332 individuals censored (40 patients transferred out, 13 patients died, 21 drop out and 258 remained till end of follow up. Therefore, the overall TB incidence rate on the follow up period calculated using Person –year of follow up was 8.64 cases per 100 Person Years. Study participants stayed in the follow up for a minimum of 0.03 month and maximum of 58.83 months. The median observation period was 46.74 months [IQR=15.95-52.42 months].The median survival time is 54.00 month. Among the TB cases occurred in the follow up period 67(56.3% were females. Majority 91(76.47%) of the cases were pulmonary TB. Forty six (38.6%) of incident TB occurred within the first months of follow up and 68(57.14%) of incident TB cases occurred within the first year of follow up.

Incident of TB is more common in urban105 (88%) of cases than the rural setting and in family size of >5 households.

Table 4: Incidence of TB and socio demographic characteristics of the study participants in Afar health facilities, northeast Ethiopia 2015

Characteristics		TB status		Total
		Censored (n=332	Event of TB(n=119	
Age	15-24	41(9.1%	14(3.1%	55(12.2%
	25-34	179(39.7%	63(14.0%	242(53.7%
	35-44	89(19.7%	30(6.7%	119(26.4%
	≥45	23(5.1%	12(2.7%	35(7.8%
Sex				
Male		132(29.3%)	52(11.5%	184(40.8%
Female		200(44.3%	67(14.9%	267(59.2%
Residence	Urban	305(67.6%	105(23.3%	410(90.9%
	Rural	27(6.0%	14(3.1%	41(9.1%
Marital status	Never married	114(25.3%	30(6.7%	144(31.9%
	Married	148(32.8%	52(11.5%	200(44.3%
	Divorced/separated	47(10.4%	30(6.7%	77(17.1%
	Widowed	23(5.1%	7(1.6%	30(6.7%
Educational level				
No formal education		157(34.8%	55(12.2%	212(47%
Primary		128(28.4%	49	177(39.3
Secondary and above		47(10.4	15(1.1%	62(13.7
Occupational status				
Self employed*		175(38.8%	59(13.1%	234(51.9%
Government employed		36(8.0%	9(2.1%	45(10.1%
No employment		121(26.8%	51(11.3%	172(38.1%
Family size				
1-3		165(36.6%	51(11.3%	216(47.9%

4-5	116(25.7%	43(9.5%	159(35.3%
>5	51(11.3%	25(5.5%	76(16.9%
Substance use			
User	88(19.5%	42(9.3%	130(28.8%
Non user	244(54.1%	77(17.1%	321(71.2%
Religion			
Muslim	205(45.5%)	70(15.5%	275(61.0%
Orthodox	118(26.2%	47(10.4%	165(36.6%
Others *	9(2.0%	2(0.4%	11(2.4%

*others =protestant, catholic …
*self employed =Merchant, house wife, daily laborer

4.4. Incidence of TB with PLHIV and their baseline clinical and follow up characteristics in Afar health facilities, northeast Ethiopia 2015.

From the study participants who developed incident TB 41(34.5%) of them had history of previous TB or treatment history and 47(39.5%) of them were either ambulatory or bedridden at enrollment. Majority 115(96.6%) of the incident cases of patients not provided with INH prophylactic therapy. Ninety five (79.9%) of participants with incident cases of TB were enrolled with Hgb level below12.5g/dl.

Table 5Incidence of TB and clinical and follow up characteristics of the study participants in Afar health facilities, northeast Ethiopia 2015

Characteristics	Categories	TB status		Total
		Censored (n=322)	event of TB(119)	
Past TB	Yes	33	41	74
	No	299	78	377
OI*	Yes	15	19	34
	No	317	100	417
Chronic illness	Yes	24	11	35
	No	308	108	416
Baseline functional status	Working	294	72	366
	Ambulatory	35	39	74
	Bedridden	3	8	11
Baseline BMI	<18.5	143	75	218
	≥18.5	161	42	203
WHO clinical stage	I	55	7	62
	II	119	29	138
	III	113	59	172
	IV	45	24	69
Baseline Hgb	<10	33	23	56
	10-12.49	142	72	224
	≥12.5	157	24	181
	<100	22	22	44
CD4cell count	100-200	84	40	124
	201-349	96	29	125
	≥350	130	28	158
	d4t-3TC-NVP	51	14	65
Initial regimen	AZT-3TC-EFV	69	20	89
	AZT-3TC-NVP	82	28	110
	TDF-3TC-EFV	118	52	170
	Others*	12	5	17
CPT use	Yes	305	108	413
	No	27	11	38
IPT	Yes	90	4	94
	No	242	115	357
Adherence	Consistent	261	90	351
	Inconsistent	71	29	100

Test of equality for survival distribution for the different levels of the different categories was performed with Kaplan Meier using the long rank test. Association of difference was observed among the explanatory variables like BMI and IPT.

Baseline BMI had a significant difference for tuberculosis –free survival as compared for people living with HIV. BMI <18.5 kg/m^2 had low TB free survival as compared to those

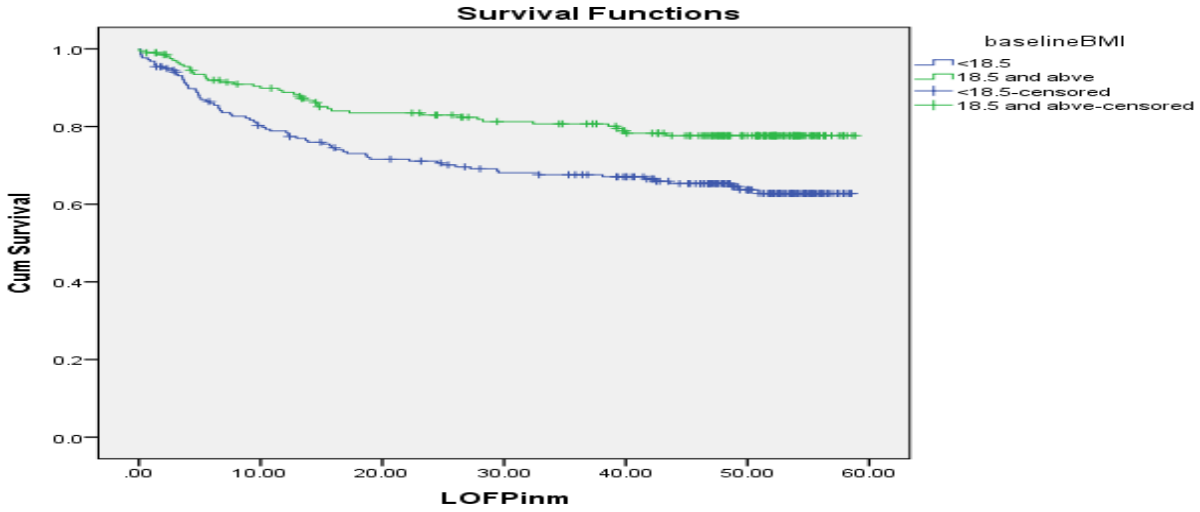

Figure 3 TB free survival probability with BMI among PLHIV in Afar health institutions northeast, Ethiopia July, 2010 –May 2015

With BMI >18.5 kg/m^2 with the overall comparison result long rank of p-value p<0.002 and for the IPT was p<0.0001 which shows significant difference of TB free survival among patients provided with IPT.

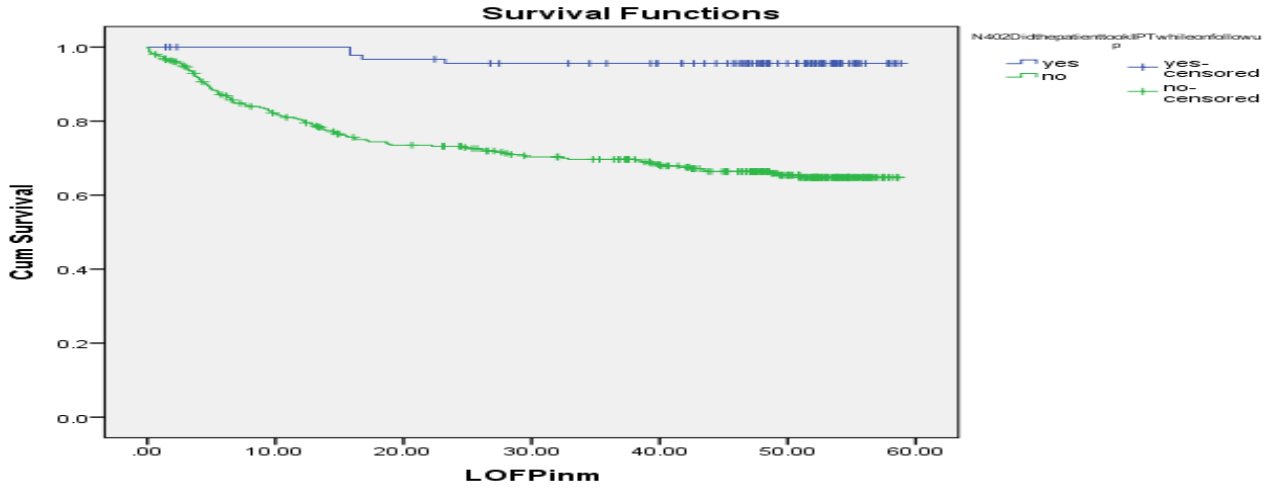

Figure 4. TB free survival probability with IPT among PLHIV in Afar health institutions northeast, Ethiopia July, 2010 –May 2015

4.4 Predictors of tuberculosis in Cox survival analysis

In a bi-variable Cox regression analysis predictors with p<0.2 value was candidate for multivariate analysis. Eleven variables were significant associated in the Bi variable analysis this were CD4 cell count, WHO clinical stage, substance use, marital status ,OI ,IPT, past TB history, BMI , Hgb ,functional status and family size were included in the multivariate analysis. The Enter and forward method was used in the multivariate analysis to see output value of the variables showed significance in bivariate analysis. Past TB history, baseline fictional status, baseline hemoglobin, baseline BMI and IPT were found statistically significant with having value of p<0.05 in multivariate analysis. According to the Cox multivariate analysis HIV patients who had history of TB at enrollment were 2.32 times risky to develop TB at a time than those who had no past TB history (AHR=2.32, 95%CI=. 2.324(1.511-3.573).Patients enrolled to care with baseline functional status of bed redden and ambulatory were 2.42 times more prone to develop TB at any follow up time than those enrolled with working functional status (AHR=2.42,95%CI(1.05-5.59) ,(AHR=2.42 ,95%CI=(1.56-3.75) respectively. Similarly, HIV patients having baseline BMI<18.5kg/m^2 were1.62 times higher risky to get TB at any time than those with having BMI≥18.5kg/m^2 at baseline (AHR=1.621, 95 %CI (1.09-2.40).HIV patient who did not take IPT were 6.96 times more likely to acquire TB at any time compared to those who taken IPT(AHR= 6.96,95%CI(2.53-19.08).in addition ,People living with HIV enrolled with baseline Hgb <12.5g/dl were 2.54 times more to develop TB at certain time than those having Hgb above 12.5g/dl respectively (AHR=2.00 ,95%(1.08-3.71) (AHR= 2.54,95%CI(1.57-4.11).

Table 6. Predictors of TB among PLHIV in Afar health facilities north east Ethiopia 2015 using Bi-variate and multivariable Cox regression

Explanatory variable	Number			
Marital status	Censored (n=322)	Event of TB(n=119)	**CHR,95%CI**	**AHR,95%CI**
Never married	114	30	1	1
Married	148	52	.942(.41-2.14)*	1.16(.69-1.94)
Divorced/separated	47	30	1.15(.52-2.53)*	1.31(.76-2.28)
Widowed	23	7	1.90(.83-4.32)*	1.55(.63-3.79)
Family size				
1-3	165	51	1	1
4-5	116	43	.718(.83-1.16)*	1.33(.85-2.08)
>5	51	25	.44(.50-1.36)*	1.54(.90-2.63)
Opportunistic infection				
Yes	15	19	2.61(1.60-4.27)*	1.270(.72-2.22)
No	317	100	1.00	1.00
Baseline Functional status				
Working	294	72	1.00	1.00
Ambulatory and bedridden	38	47	.199(.096-.414)*	**2.42(1.56-3.75)****
BMI				
<18.5	143	75	1.80(1.23-2.63)*	**1.62(1.09-2.39)****
≥18.5	161	42	1	1
WHO clinical stage				
I	55	39	1	1
II	119	29	.280(.121-.651)*	1.32(.57-3.06)
III	113	59	.489(.285,.840)*	1.90 (.84-4.29)
IV	45	24	1.00(.628,1.621)*	1.91(.78-4.65)
Hgb				
<10	33	23	4.12(2.32-7.32)*	**2.00(1.08-3.71)****
10-12.49	142	72	2.97(1.87-4.71)*	**2.54(1.57-4.11)****
≥12.5	157	24	1	1
CD4 cell count				

Table 2. Predictors of TB among PLHIV in Afar health facilities north east Ethiopia 2015 using Bi- variate and multivariable Cox regression result continued.

<100	22	22	4.12(2.35-7.22)*	1.33(.68-2.61)
100-200	84	40	2.13(1.31-3.46)*	1.56(.89-2.73)
201-349	96	29	1.44(.85-2.42)*	.93(.535-1.62)
≥350	130	28	1	1
IPT Use				
Yes	90	4	1	1
No	242	115	.106(.03-.28)	**6.96(2.53,19.08)*****

*p-value <0.2, **p-value<0.05 in multivariate. ♣=p-value <0.2

***p-value <0.001 in multivariate, 1=reference category

Global test of proportional hazard assumption for predictors fitted to Cox proportional hazard model was not significant

5. DISCUSSION

It is universally acknowledged fact that HIV infection increases the incidence of tuberculosis. TB and HIV remains as major public health problems in many parts of the world. The fact that, Ethiopia is among the TB high burden countries with an estimated annual incidence of 211case per 100,000 populations and with prevalence of 224 cases per 100,000(4).TB is the most common cause of morbidity and mortality among PLHIV.HIV infected individuals 20-37 times greater risk to develop TB in life time compared to non infected individuals(7, 8).

This study tried to assess the overall incidence of TB among the participants for the entire follow up period. It was found to be 8.64 cases per 100 person years. This finding was consistent with studies conducted in Ethiopia which founds (7cases /100 PY and 7.9 cases per/100 PY)(23, 25). It also aggresses with findings from Tanzania7.9 (95% CI), 7.6-8.2] per 100 and Sub-Saharan Africa (21, 22). However, it was high as compared to studies conducted in Korea, Israel and Malaysia (16, 17, 19). This could be explained by the fact that these countries might have better preventive, diagnostic and treatment setups and strategies for controlling TB in contrast this study was done in a high TB burden country and scarce resources might contribute for this high result. Low health care coverage and late enrollment to health care facilities might contribute for this finding. This could be also explained with progression of the latent infection to active TB after initiation of HIV chronic care with late presentation of patients to health facility. The patient might get new infection or IRIS after initiation of HAART and other HIV related services. IRIS associated TB was commonly seen within the first 6 months after initiation of HAART (15).

In different studies multiple predictors can predict the incidence of TB among PLHIV on HAART and Pre HAART era. Our study found that past TB treatment history, non use of IPT, baseline functional status of bedridden and ambulatory, low baseline Hgb level and low baseline BMI were significantly associated with increased risk for acquiring TB in the study participants.

This study revealed that HIV infected individuals with Past TB history had 2.3 times high risk to develop TB as compared with HIV individuals with no have past TB history. Our finding was similar with findings from studies done in Israel and Malaysia and Uganda (16, 17, 38). The possible explanation could be due to poor compliance for their anti TB treatment at first episode and it could be due to relapse .Reactivation or re-infection might also possible with the existing dysregulated immunity.

Participants not provided with IPT were 7 times higher risk to develop TB as compared to individuals who took IPT (AHR=6.96,95%2.53-19.08).This study found that IPT were independent risk factor associated with occurrence of incident TB among adult HIV patients. This is consistent with studies done in Ethiopia, South Africa and Brazil (24, 34, 35). In fact, IPT is recommended to reduce and control TB among this group of people. Despite the fact, the poor uptake and the ambiguity and fear of drug resistance might contribute for these participants non- IPT user. This is an alarming to scale up the IPT on the setting.

Patients' ambulatory and bedridden functional status at baseline is 2.42 times more likely to develop TB in the entire follow up as compared to working functional status. This finding is in line with other study done in northwest Ethiopia(23). The possible explanation was debilitated patients prone to malnutrition and less physical activity that make them prone for many diseases and TB.

Patients with BMI of <18.5 at baseline was 1.62 times higher risk of developing TB as compared to adults with BMI≥18.5 at base line. This finding was consistent with phase III randomized controlled trial study done in Tanzania(30).It was also agrees with studies done in Ethiopia and south Africa (21, 40). The possible explanations, low BMI is a sign of malnutrition.HIV patients are prone for malnutrition. Malnutrition in HIV patients associated with increased catabolic activity, infection and loss of appetite and decreased in take. This all contributes for low BMI. Malnutrition is one of the pertinent risk factor of TB among HIV and non HIV patients.

Similarly this study found that patients with Hgb level of <10 and 10-12.5 at base line were 2.00 and 2.54 times higher risk of developing TB than those having Hgb level

>12.5 at base line. Hematologic complications were risk factors for the incidence of TB among PLHIV .This finding was in line with studies conducted in Ethiopia, Uganda and Tanzania south Africa(30, 32, 33, 40). The Possible explanation is malnutrition and side effect of medications, opportunistic infections and advanced stage of the disease. Undiagnosed TB could explain the low Hgb level at the early enrollment. Variables like CD4 cell count and WHO clinical stage were not independently associated in this study.

6. Strength of the study

The study tried to include all possible variables that influences risk of TB among HIV patients that could accessed from the chart. The study was conducted for a five year follow up that helps to show the long term impact of HIV on TB.

7. Limitation of the study

This study might have limitations that shared with limitation of most retrospective record based studies had. The retrospective and record based nature of the study design limited to include predictors that could affect the risk of TB like housing condition, house hold income and other. Due to incomplete data some study subjects were removed from the study that might undermine the finding if those study subjects had TB. The study not observed ART group and Pre ART group separately.

8. Conclusion

The overall incidence of TB in the study setting is high. HIV infected individuals with history of previous TB, not using IPT, base line BMI<18.5kg/$m^{2,}$ ambulatory and bedridden functional status and having baseline Hgb <12.5g/dl were most predictors of incident TB.

9. Recommendation

For governmental organizations and stakeholders:

- Strengthen the TB /HIV collaborative activity
- Giving trainings on the provision of IPT that might Strengthen the strategies for prevention and control of TB among adult HIV infected people
- Close supervision for Implementation of the guidelines and standards strategies to prevent and control TB.

For health professionals:

- ✓ Strength the provision of IPT and nutritional support to all eligible HIV individuals
- ✓ Continuous follow up and early detection of malnutrition, prevention of other infection and close monitoring for HIV patients enrolled with ambulatory or bedridden functional status and low BMI <18.5and low Hgb at baseline to control TB among this groups.

For patients

- ✓ Patients would be encouraged to have improved treatment and care seeking and infection control behavior.

For researchers:

- ✓ Further prospective studies might need to include all factors that influence the risk of TB.

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11. Annex

Annex-1 Information Sheet and Consent Form

Title of the Research Project: Incidence and predictors of tuberculosis among people living With HIV/AIDS in Dubti General Hospital , Asayta Hospital, Abala hospital , Awash and samara health centers, Afar region, Northeast Ethiopia, 2015.

Name of Principal Investigator: Ausman Ahmed

Name of the Organization: University of Gondar, College of Medicine and Health Science, Department of Internal Medicine.

Introduction This information sheet is prepared for ARHO, Dubti General Hospital administration and Dubti hospital, Asayta and Abala hospital chronic HIV care clinic focal person and the health centers. The aim is to explain about the purpose of the study and the procedure of data collection. Moreover, to obtain permission and cooperation to done the research.

Purpose of the Research Project: The study is aim to assess the incidence and predictors among adult people living with HIV/AIDS who enrolled in chronic HIV follow up clinic at Dubti General Hospital ,Asayta hospital and three health centers ,Afar region, Northeast Ethiopia, 2015.

Risk and/or Discomfort: By participating in this research project no one patient will be harmed because the information is extracted from secondary data. Also, during data collection name or any unique patient identifying information will not recorded on the data collection format and the collected data will be kept confidential and security will be assured.

Benefits: Participating in this research have no direct benefit for those individuals whose chart is included in the study but the indirect benefit is quite important for the participants ,other patients and for a community as a whole. This helps us in showing the appropriate action to pick up the determinants and to take a right measure in providing appropriate ways in strengthening the collaborative activities in TB/HIV care and treatment service provision.

Incentives for Participating: data will be collected from patient charts and no need of providing any incentive to any one taking part in this study.

Confidentiality: The information collected from the chart will kept confidential. The extracted information will not include unique patient identifying information or name. The data will be collected by trained professionals and confidentiality of information will secure safely and data will be stored in a file and locked with private password. Such information will not be revealed to anyone except the principal investigator.

Person to contact: The research project will be reviewed and approved by the Institutional Review Board of College of Medicine and Health Sciences, University of

Gondar. In case, if you want to know more information about the research and its undertakings, you can contact any one of the following persons through the address below**.**

Ausman Ahmed

Tell: 0910426480, E-mail:soyra3362@yahoo.com

Mr. Melaku Kindie (BSc, MPH), University of Gondar, College of Medicine and Health Science, Institute of public health.

Tel: 0913002871

1. Dr. Desalew Mekonnen (MD, Assoc prof of Internal medicine)**,** University of Gondar, College of Medicine and Health Science department of internal medicine.

   Tel:

Annex 2: English Questionnaire format

Afar National Regional State, Dubti Hospital, Asayta hospital, Awash, Logia and Samara health centers

Data collection format

Activity and responsible body	Response
Questionnaire Code	
Name of the health institutions	
Date of data collected	DD/MM/YYYY/ _____/_____/_____
Name of Data Collector	
Supervisor Name	Signature_____Date_____

Checked by Investigator: Signature _____Date _____

Ser .No	Part I:**socio demographic characteristics**		Skip pattern
101	Date of enrollment	__/___/____ DD/MM/YY	
102	Age in years	____year	
103	Sex	1.Male 2.Female	
104	Level of education	1.No formal education 2.Primary 3.Secondary 4.More than secondary 5.Not recorded	
105	Residence	1.Urban 2.Rural	
106	Substance abuse	1.Khat 2.Tobacco 3.Alcohol 4.Drugs 5.not use	
Part II: HIV and Follow up related characteristics			
201	Did the patient had past TB history?	1.Yes 3.not recorded 2.No	If #201 is2 or 3→203
202	Does the treatment completed?	1.yes 2.No	
203	Does the patient develop opportunistic infection (not TB)	1.Yes (specify)____ 2.No	
204	What was baseline Hgb level	_____	
205	What was baseline BMI	Height --------cm Weight _____kg BMI=w/h^2_____	
206	Does the patient has chronic illness	1.yes (specify) _____ 2.No	
207	Functional status of the patient	1.working 2.Ambulatory 3.Bed redden	
208	Baseline WHO clinical stage	1.I 2.II 3.III 4.IV	
209	Baseline CD4 cell count	_____	

Part III: Treatment and Follow up related characteristics			
301	ART eligible date	__/__/__ DD/MM/YY	
302	Eligibility criteria	1.CD4 cell count 2.WHO clinical stage 3.Both 4.T-cell lymphocyte count	
303	Date ART started	__/____/_____ DD/MM/YY	
304	Initial regimen	1.d4t-3TC-NVP 2.d4t-3TC-EFV 3.AZT-3TC-NVP 4.AZT-3TC-EFV 5.TDF-3TC-EFV 6.TDF-3TC-NVP 7.ABC-3TC-NVP 8.ABC-3TC-EFV	
305	Did the regimen changed?	1.yes 2.not yet 3.Not recorded	
306	What was the reason for change?	1.TB 2.pregnancy 3.side effect 4.Failure 5.Not recorded	
307	What was new regimen started?	1.d4t-3TC-NVP 2.d4t-3TC-EFV 3.AZT-3TC-NVP 4.AZT-3TC-EFV 5.TDF-3TC-EFV 6.TDF-3TC-NVP 7.ABC-3TC-NVP	

		8.ABC-3TC-EFV 9.second line regimen	
308	Adherence status	1. consistent 2. inconsistent	
309	Did the patient take CPT?	1.yes 2.No	
310	Did the patient take IPT?	1.Yes 2.No	If no→315
411	Did the patient develop TB while she/he is on follow up	1.yes 2.no	
412	When was it developed?	--/--/--- DD/MM/YY	
413	During what was it happen?	1.Pre-ART time 2.On ART time	
414	What form of TB was it?	1.pulmunary (specify) 2.Extra pulmonary 3.Both 4.MDR TB	
415	Last follow up date	……. DD/MM/YY	
416	Status at last follow up	1.Alive 2.Transfer out 3.Deid 4.Drop out	

Annex 3: Declaration

The undersigned Msc student agrees to accept responsibility for the scientific, ethical and technical conduct of the research project and for provision of required progress reports as per terms and conditions of the research and publications office of the University of Gondar.

Name of the student: - Ausman Ahmed

Date:_____ Signature: _____

This thesis report has been submitted for examination with my/ our approval as university advisor (s)

Advisors:

Name	Signature	Date
1. Mr. Melaku Kindie (BSc, MPH)	_____	_____
2. Dr. Desalew Mekonnen (MD+, Assoc Prof Internal medicine)	_____	_____